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GLASS-BASED BIOMATERIALS: PRESENT AND FUTURE (A REVIEW)

E. E. Stroganova,[1] N. Yu. Mikhailenko,[1] and O. A. Moroz[1]

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The main trends in the development of a wide range of bioactive materials for medical purposes based on glasses are considered. Such materials are classified based on their compositions, physicochemical properties, and their relations to body tissues.

Contemporary medicine with increasing frequency and success practices surgery substituting artificial tissues for injured organs and thus grants normal life to thousands of patients. This is related to the development of unique diagnostic methods allowing for detecting a disease at an early stage and also to a constant expansion of the list of available synthetic materials acting as substitutes for blood vessels, cartilages, soft and bone tissues.

The main purpose of surgery in early 20th century was saving lives of patients at the cost of removing injured tissues and organs. After the development of transplant surgery, it has become possibility to extend normal functioning of injured organs by their full or partial substitution.

[1] D. I. Mendeleev Russian Chemical Engineering University, Moscow, Russia.

L. L. Hench, one of the founders of the theory of bioactivity of synthesized materials and one of the first researchers developing bioactive glass compositions, distinguishes two stages in the development of artificial materials intended for replacement of damaged tissues and organs (Fig. 1) [1].

According to L. L. Hench's classification, materials currently used for bone endoprostheses are divided into two groups, namely, transplants that are natural materials obtained from human or animal donor bone and soft tissues, and implants, i.e., artificial materials synthesized on the basis of organic and inorganic natural materials.

The first group of materials involves a multitude of problems related to procurement, treatment, and storage of donor tissues etc. At the same time, materials of this group have the structure and properties of natural tissues and in a case of

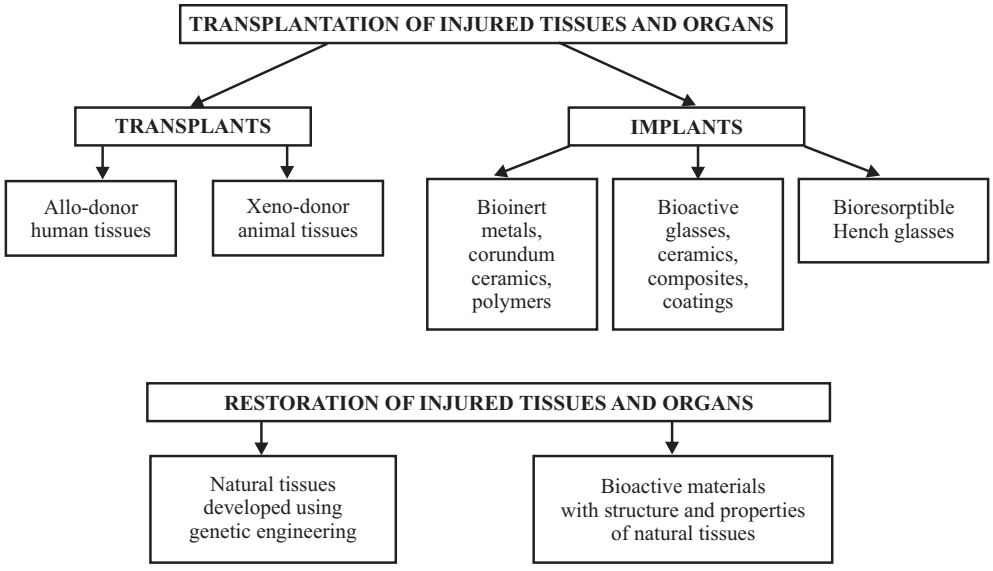

Fig. 1. Classification of biomaterials.

prompt procurement and appropriate treatment their application gives good results. The evolution of world bioimplantology is directed to the expansion of available xeno- and allo-tissue implants, their saturation with biologically active components (growth factors, glycosamine-glycans, morphogenetic proteins, etc.), and development of articles combining synthesized and biological materials [2].

Materials of the second group, which includes metals, ceramics, graphite, polymers, glass, glass ceramics, and composite materials and coatings, are successfully used when properties of materials correspond to the properties of tissues replaced, and according to physicians' estimates, their life in an organism on the average lasts 10 – 15 years [3, 4].

In using bioinert materials, when an endoprostheses is implanted into a growing bone or a bone with modified properties (elderly patients), surgery often needs to be repeated due to corrosion of the implant under the effect of the body medium or destruction of adjacent bone tissues due to discrepancy of properties of the material and the bone.

It has become possible to solve this problem when a new class of synthesized materials called bioactive was developed. Bioinert material in contact with bone tissue becomes encapsulates in connective tissue preventing its close contact with the bone, which is another reason for repeated surgeries. In contrast, bioactive materials, i.e., glasses, glass ceramics, and ceramics containing a bioactive component do not become encapsulated, closely adhere to surrounding bone tissues, and stimulate growth of new bone, which is called osteogenesis [5].

Various requirements are imposed on medical materials, including technological parameters, physicochemical characteristics, and biological properties taking into account various aspects of interaction of implant material with the body medium. The most general requirements related to bone transplant and implants can be formulated as follows [6]:

– absence of allergic, toxic, inflammatory and other undesirable reactions of adjacent tissues to implant materials;

– correlation of properties of material implanted with properties of bone replaced;

– possibility of treating implants by traditional sterilization techniques,

– x-ray contrast of materials implanted allowing for monitoring its behavior in service.

The first reports on bioactive materials based on glasses appeared in 1970-s in studies of L. L. Hench, W. Vogel, T. Kokubo [7 – 9]. These studies were focused on the development of glass and glass ceramic compositions based on silicate systems, in which small additives of calcium and phosphor oxides ensured bioactive properties, whereas a vitreous or a glass-ceramic silicate matrix containing crystalline phases (phlogopite, diopside, wollastonite) ensured mechanical properties.

At the same time, possibilities of obtaining bioactive materials based on phosphate glasses were investigated and composite materials produced, in which bioactive glasses were tested as fillers for a collagen or a polymer matrix [10 – 16]. Another intensely developing line of research was deposition of bioactive coatings on extended metal endoprostheses in order to increase their strength of adhesion to adjacent bone [17, 18].

The main purpose of researchers in those years was to obtain glass ceramic materials combining a maximum strength, comparable with the strength of commonly used bioinert materials (metals and corundum ceramics), and bioactivity. To accomplish this purpose, such well known techniques as powder technology of glass ceramics, strengthening additives of zirconium oxide modified by yttrium oxide, and unidirectional growth of wollastonite crystals and chain calcium phosphates [19 – 22] were used. In this way it became possible to obtain materials with bending strength of 200 – 600 MPa preserving the capacity of intergrowing with adjacent bone (Table 1).

Despite the strength parameters attained, the developed materials could not compete with metals under high dynamic loads. Furthermore the majority of glass ceramics materials are difficultly soluble and therefore only able to form a surface bone layer connecting the implant and the bone (the strength of bond ranging from 2 to 5 MPa) [6].

For clearer understanding of processes occurring in the zone of a material – bone contact, a series of experiments was carried out focused on the behavior of various materials (silicate and phosphate glasses and glass ceramics) in artificial media simulating *in vitro* the human physiological medium and blood plasma and experiments *in vivo* in contact with soft and bone tissues tested on animals.

The results obtained pointed to numerous simultaneous reactions occurring in the intermediate layer between the bone and the implant with participation of the surface layer of the implant and the ambient physiological medium. As a consequence of studies performed [3, 6 – 7, 27, 28], a scheme of interaction was proposed describing the sequence of processes on the surface of material (Fig. 2).

It should be noted that such scheme of bone structure formation is true for silicate systems and a prerequisite for successful process is a silica gel substrate actively absorbing ions of alkali and alkali-earth cations, as well as phosphate and carbonate anions groups, i.e., building material for a new bone structure.

For phosphate systems, reactions directed to the formation of the apatite structure corresponding to reactions (1) – (6) in Fig. 2 proceed according to different schemes depending on the composition of dissolving material. In studying the processes of dissolution for glasses of the $CaO – R_2O – P_2O_5$ system (where R is used for Na and K) in water and in the physiological medium depending on the ratio $CaO : P_2O_5$, the following reactions were registered [29]:

$$CaHPO_4 \rightarrow DefHA \rightarrow HA;$$

$$Ca_2P_2O_7 \rightarrow DefHA \rightarrow HA;$$

$$Ca_8(HPO_4)_2(PO_4)_4 5H_2O \rightarrow DefHA \rightarrow HA,$$

TABLE 1

Material	System	Properties	Published source
Bone	$CaO - P_2O_5$ and small additives	σ_c = 90 – 170 MPa $\sigma_{b=}$ 120 – 180 MPa E = 15.5 – 18.0 GPa	[23]
	Materials based on silicate systems		
Bioglass®	$SiO_2 - Na_2O - CaO - P_2O_5$	σ_b = 42 MPa E = 35 GPa	[7]
Ceravital®	$CaO - P_2O_5 - SiO_2$, additives Na_2O, K_2O, MgO	σ_b up to 150 MPa	[24]
Cerabone®	$CaO - P_2O_5 - SiO_2$, additives MgO, CaF_2	σ_b = 178 MPa $\sigma_{b\ nitr}$ = 215 MPa σ_c = 1060 MPa E = 117 GPa $K_{1C} = 2.0\ MPa \cdot m^{1/2}$	[8]
Bioverit®	$Na_2O - MgO - CaO - Al_2O_3 - SiO_2$, additives P_2O_5, F_2	σ_b = 178 MPa $\sigma_{b\ nitr}$ = 215 MPa σ_c = 1060 MPa E = 117 GPa $K_{1C} = 2.0\ MPa \cdot m^{1/2}$	[9]
	Materials based on phosphate systems		
Aluminum-bearing	$CaO - P_2O_5 - Al_2O_3$	σ_b up to 100 MPa	[10]
Niobium-bearing	$CaO - P_2O_5 - Nb_2O_5$, additives Al_2O_3	σ_b = 70 – 130 MPa E = 76 GPa	[11]
Biositall KF	$CaO - P_2O_5 - Al_2O_3$, additives B_2O_3, TiO_2, ZrO_2	σ_b = 100 – 160 MPa E = 75 GPa	[12]
	Materials with increased strength		
Cerabone® strengthened	$CaO - P_2O_5 - SiO_2$, additives MgO, $CaF_2 + ZrO_2$, modified I_2O_3 and Al_2O_3	σ_b = 440 – 480 MPa $\sigma_{b\ nitr}$ = 480 – 550 MPa $K_{1C} = 2.3 - 2.8\ MPa \cdot m^{1/2}$	[20]
Calcium-phosphate glass ceramics	$CaO - P_2O_5$ – calcium meta-phosphate (oriented crystals)	σ_b = 640 MPa E = 85 GPa Stepwise destruction	[22]
	Composite materials		
Composite cellular biomaterial BAK	HC glass, hydroxyapatite powder	Open porosity 10 – 80% σ_b = 10 MPa σ_c = 20 MPa	[25]
Material for transporting medications	Cerabone® + bis-HMA/TEHDMA	σ_c = 68 – 110 MPa	[14]
Glass-ionomer cement with bioactive fibers	$CaO - P_2O_5 - SiO_2 - Al_2O_3$ – fibers + HY-BOND Glassionomer CX	σ_c = 35 MPa Setting duration up to 11 min	[15]
Material for transporting medications	$SiO_2 - CaO - P_2O_5$ (glass) + PMMA (matrix)	Rate of exit of medication is equivalent to the rate of ion exchange reaction $Ca^{2+} \leftrightarrow H_3O^+$	[26]
Bioresorptive composite	Bioglass® + polyethylvinyl alcohol	σ_{tens} = 36.8 MPa E = 3.8 GPa	[25]
Bioverit® with strengthening additives	$Na_2O - MgO - CaO - Al_2O_3 - SiO_2 - P_2O_5 - F_2 + ZrO_2$, pure and modified I_2O_3	σ_b = 50 – 95 MPa σ_c = 118 – 230 MPa E = 59 – 78 GPa $K_{1C} = 1.7 - 2.5\ MPa \cdot m^{1/2}$	[21]
	Bioactive coatings		
Solid titanium and titanium mesh	Biositall KF (plasma spraying), glass ceramic coating	Thickness 150 – 300 μm σ_{destr} up to 20 MPa	[17]
Titanium and silicon	$CaO - P_2O_5 - SiO_2 - MgO$ (magnetron spraying), glass ceramic costing	Thickness 100 – 700 μm σ_{destr} up to 57 MPa	[18]

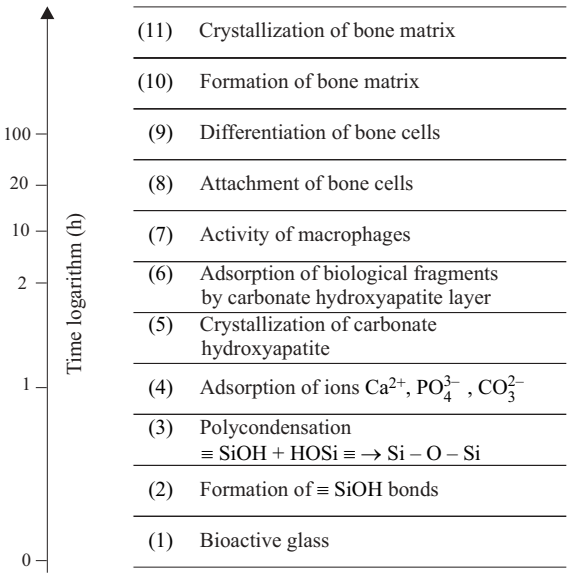

Fig. 2. Phases of surface reactions.

where DefHA is nonstoichiometric hydroxyapatite; HA is stoichiometric apatite.

Subsequent formation of bone structure with participation of organic compounds proceeds in accordance with data in Fig. 2.

A criterion of bioactivity of glass-based materials can be the rate of formation of an amorphous apatite layer on the surface of the implant in *in vitro* tests. For *in vivo* tests, the bioactivity index is used, $I_b = 100/\tau_{0.566}$ ($\tau_{0.566}$ is the time in which half of the surface area of the implant becomes bonded to the adjacent bone) and the class of bioactivity reflecting the capacity of a material to react with different types of tissues. Table 2 lists materials attributed to different classes of bioactivity [1].

In accordance with these notions, the phase diagram of the $CaO – SiO_2 – P_2O_5$ system indicates glass-formation areas, in which vitreous and glass ceramic materials with different capacities for contact with soft and bone tissues can be obtained (Fig. 3).

The main achievements in the field of development of bioactive glass and glass ceramic compositions and studying

TABLE 2

Biomaterial	Bioactivity index	Bioactivity class	Capacity of bonding with tissues	
			bone	soft
Bioglass®	12.5	A	Exists	
Cerabone®	6.0	B	Exists	None
Ceravital®	5.6	B	Exists	None
Hydroxyapatite ceramics	3.1	B	Exists	None
Corundum ceramics	0	0	None	

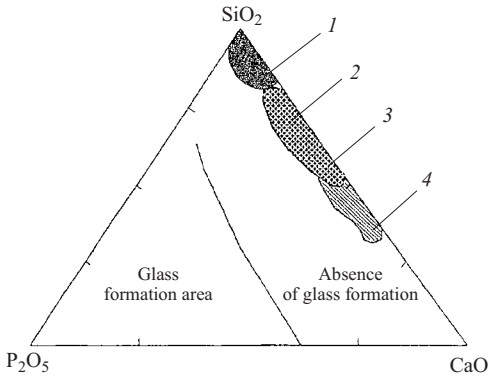

Fig. 3. Classification of bioactive glasses: *1*, *3*, and *4*) formation of apatite layer on gel glasses after 7 – 20 days (class B), 1 – 3 days (class A) and 7 days (class B), respectively ; *2*) bioresorption in the process of bone regeneration (class A).

their interaction with body tissues can be formulated as follows:

– the ranges of existence of bioactive material compositions of classes A and B based on glasses of systems $CaO – SiO_2 – P_2O_5$ and $CaO – SiO_2 – Na_2O$ are identified:

– variation limits of main physicochemical properties, such as strength, elasticity modulus, and chemical resistance of these materials are identified;

– the regularities of implants bonding with bone are established and the effect of the composition of material and pH of the medium on the rate of formation of an amorphous hydroxyapatite layer on the implant surface is determined;

– it is demonstrated that successful growth of bone tissue in the intermediate layer between an implant and a bone requires the formation of a layer of hydrated amorphous silica in silicate system and the formation of hydrated calcium phosphates in phosphate systems.

The results obtained made it possible to determine the main directions of research for the development of next generations of bioactive. materials capable of modifying their structure and properties as a consequence of reactions with tissues of an organism after surgery.

For materials of class A this means regulation of the rate of growth of new tissues by means of cultivation of cell cultures on their surface *in vitro*. By varying the composition of material, it is possible to suppress the growth of some cell structures and initiate the growth of others [29].

For materials of class B this means modification of the material from a compact structure to a porous one or development of active centers (silica gel or amorphous hydroxyapatite layer) on its surface. The advantages of porous implants compared to compact ones consists in the fact that when bone tissue grows through such material, it becomes reinforced, which has a significant effect on the strength parameters of the implant itself and its bond with the bone [29, 30]. Modification of surface properties of implant, for instance, by pickling sintered glass ceramics AW in hydrochloric acid until the formation of a silicic acid layer and

subsequent treatment in an artificial plasma solution accelerates several times the process of bonding of the implant with the bone after surgery [31].

Surface activation methods developed for bioactive materials (pickling in solutions of mineral alkalis and acids, exposure in solutions simulating physiological media and blood plasma, planting various cell cultures on a porous surface) were tested on bioinert materials: silicate glasses, titanium and tantalum implants, as well as glasses with a high content of silicon oxide obtained according to the sol-gel technology. They all have capacity for interacting with body tissues and the use of sol-gel technology makes it possible to control the structure of such materials at the nanolevel.

The existent bioactive materials based on glass are intended for use in restoration and substitution surgery as bioactive coatings for extended endoprostheses, porous and granulated implants for correction of bone defects, systems for delivery of medicinals, and for light-curing and chemically curing composites in dentistry.

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